REMARKS

This amendment is responsive to the Office Action mailed February 6, 2007. Withdrawn Claims 1-3 and 15-35 have been previously cancelled. Claims 4, 5, 8, and 9 have been cancelled herein. Claims 6, 7, 10, 12-14, and 36-39 are currently pending.

Applicants acknowledge with appreciation the Examiner's withdrawal of the rejections presented under 35 U.S.C. §112 as well as the withdrawal of the rejections presented under 35 U.S.C. §102 as anticipated in view of Look et al., *Antiviral Research*, 43:113-122 (1999) and international publication WO 99/67362 to Rumin et al.

Claims 6 and 7 have been amended herein to specify a method for inhibiting or downregulating Hepatitis C viral replication. Support for the amendment can be found throughout the specification, *see, e.g.*, Example 14 on pages 36-37.

Similarly, Claim 10 has been amended to now depend from Claim 6. The dependencies of Claims 12-14 have also been corrected in view of the cancellation of claims. No new matter is presented.

Applicants thank the Examiner for her telephone call on January 30, 2007. During the teleconference, the Examiner indicated that she still considered the claims to be anticipated in view of the art provided by the Applicants in the IDS submitted July 25, 2006; however, the Examiner indicated that claims specifically directed to inhibiting or downregulating Hepatitis C *viral replication* appeared to be allowable over the prior art of record. The Examiner proposed the following amendments made herein and requested that Applicants file a supplemental amendment and/or authorize an Examiner's amendment; however, the undersigned attorneys of record were unable to attain authorization for the claim amendments within the Examiner's requested timeline and therefore this final Office Action was issued on February 6, 2007.

It is believed the amendments made herein address and obviate all remaining issues in this case. However, in order to be completely responsive to the Office Action, Applicants address the issues presented below.

Since the requested amendments are in response to the Examiner's request, Applicant believes the amendments fall within the definition of amendments "complying with any requirements of form expressly set forth in a previous Office action" as set forth in 37 C.F.R. §1.116. Alternatively, since the amendments more clearly and particularly point out that which Applicant regards as his invention, Applicant requests entry of the amendments as "presenting rejected claims in better form for consideration on appeal", also as set forth in 37 C.F.R. §1.116.

Entry of the amendments and allowance of the application are respectfully requested.

Response to issues presented under 35 U.S.C. §102

In the Office Action, Claim 9 has been rejected under 35 U.S.C. §102(b) as being unpatentable over Chu et al., *Journal of Nutrition*, 129: 1846-1854 (1999) (hereinafter "Chu"). Specifically, the Examiner contends that Chu teaches:

> "a method of induction of a Gpx2 gene expression in a mammalian cell lines including the epithelial cells of gastrointestinal (GI) tract by incubating the cells in the presence of selenium salt and retinoid acid (RA)" (Office Action, page 3)

Applicants note that Claim 9 has been cancelled herein and therefore the rejection is moot. Furthermore, the remaining claims have been focused to methods for inhibiting or downregulating Hepatitis C viral replication, which is not taught or suggested by Chu. Accordingly, in view of the amendments herein, withdrawal of the rejection under 35 U.S.C. §102(b) is respectfully requested.

Response to issues presented under 35 U.S.C. §103

Esworthy in view of Chu

In the Office Action, Claim 8 has been rejected under 35 U.S.C. §103(a) as being obvious over the combination of Esworthy et al., *Biochemica et Biophysica Acta*, 1381:213-226 (1998)(hereinafter "Esworthy") and Chu et al. Chu et al. is applied identically as recited above. The Examiner cites Esworthy as teaching that glutathione peroxidase or its mRNA is induced and up-regulated by selenium in a dose-dependent manner. The Examiner alleges it would have been obvious to a person skilled in the art to combine the teachings to further promote the expression and activity of glutathione peroxidase to prevent oxidative stress.

Once again, consistent with the amendments proposed during the teleconference between the Examiner and Applicants' representative, Claim 8 has been cancelled herein and therefore the rejection is moot. The remaining claims have been focused to methods for inhibiting or downregulating Hepatitis C viral replication, which is not taught or suggested by Esworthy or Chu, alone or in combination. Accordingly, in view of the amendments herein, withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

Combination of Hellstrand, Ablrecht, Esworthy, Reddy, and Chu

Similarly, Claims 4-7, 10, 12-14 and 36-39 are rejected as obvious over the combination of: US Patent No. 6,242,473, issued to Hellstrand et al.(hereinafter "Hellstrand"); US Patent No. 6,172,046,

issued to Albrecht et al.(hereinafter "Albrecht"); Reddy et al., *Hepatology*, 33:433-438 (2001) (hereinafter "Reddy"); and Chu et al. and Esworthy et al. noted above.

The Examiner states:

> "The claims 4-7, 10, 12-14 and 36-39 are directed to a method for treating HCV infection and **its associated disease** by administration of selenium or selenium salt in combination (with) a retinoic or retinoic acid salt to the cell culture or to an individual...it would have been obvious for a person having ordinary skill in the art at the time of the invention was filled to be motivated by combining the method taught by Hellstrand et al. in view of Chu et al. Esworthy et al. and further adapting the method taught by Albrecht et al. in light of Reddy et al. to get an improved therapeutic effect against disease caused by HCV infection. Because the art prior to the application was filed had already taught that selenium, glutathione peroxide and retinoid compounds can be used for treating the disease caused by HIV (sic, HCV) infection, and up-regulation of glutathione peroxidase in the GI tract can be achieved by selenium and retinoid acid compound together." (Office Action, paragraph bridging pages 5 and 6, emphasis in original)

Foremost, Applicants note that Claims 4 and 5 have been cancelled and Claims 6, 7, as well as Claims 10, 12-14, and 36-69 through their dependency from Claims 6 or 7, have been amended herein to specify methods for inhibiting or downregulating Hepatitis C viral replication in an individual or cells. As taught in Applicants' specification, treatment of HCV replicon cells with all-trans-retinoic acid led to a two- to five-fold reduction in the expression of subgenomic HCV RNA and of viral protein NS5a. *See*, page 37, lines 7-20, of Applicants' specification.

MPEP §2143.03 states that "[t]o establish *prima facie* obviousness of a claimed invention, all claim limitations must be taught or suggested by the prior art." (emphasis added) Obviousness cannot be established using Applicants' own disclosure as a guide to merely selecting and reconstructing the claimed invention from elements scattered in the prior art. *In re Dance*, 160 F.3d 1339, 1348, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998).

Hellstrand is directed to the treatment and prevention of reactive oxygen metabolite-mediated (ROM) damage by administering a ROM scavenger, *e.g.*, glutathione peroxidase. Hellstrand also suggests that minerals such as selenium and manganese can also be efficacious in combating ROM-mediated damage. Hellstrand has a "predictive", *i.e.*, prophetic, example of treating *symptoms of* Hepatitis C. As noted in Hellstrand, in HCV infected patients, damage to the patients' liver tissue is due to both the virus and the patients' immune response:

> "Liver damage caused by phagocytic cells results, in part, from ROM

> production. The presence of the ROMs can also block, inhibit or prevent lymphocytic cells from effectively dealing with the source of the infection." (Hellstrand, column 15, lines 50-54)

Hellstrand then "predicts" in a prophetic example not actually conducted, that the administration of histamine and vitamin E to a patient would:

> "serve to eliminate or inhibit direct ROM mediated damage, and also function to facilitate and enhance NK cells and T-cells so that they respond better to the viral infection." (Hellstrand, column 16, lines 45-54, and column 15, lines 56-59)

However, there is no teaching or suggestion in Hellstrand of methods of inhibiting or downregulating Hepatitis C viral replication in an individual or cells comprising the administration of a selenium or selenium salt and a retinoid. This lack of teaching is not cured by the combination of Albrecht, Reddy, Esworth and/or Chu.

Albrecht teaches a method of treating chronic hepatitis C infection using a combination therapy of ribavirin and a therapeutically effecting amount of interferon-alpha.

Reddy teaches that a once weekly regimen of pegylated (40-kd) Interferon α-2a offers superior efficacy to a 3-times-weekly regimen of IFN α-2a in the treatment of chronic Hepatitis C viral infection.

Chu teaches that the expression of selenium-dependent glutathione peroxidase can be regulated by retinoic acid.

Similarly, Esworthy teaches that expression of glutathione peroxidase is induced in a dose-dependent manner by the administration of selenium.

Taken individually or together, Hellstrand, Albrecht, Reddy, Chu, and Esworthy only provide unrelated examples of improved interferon or ROM therapy for HCV patients or a discussion of the transcription/translation regulators for glutathione peroxidase. They provide no insight, however, for solving the technical problem addressed by Applicants' invention, *i.e.*, how to inhibit or downregulate Hepatitis C viral replication in an individual or cells.

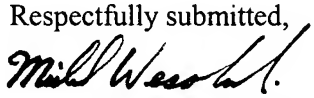
Accordingly, the invention as claimed in Claim 6 and 7 include limitations neither found in nor suggested by the prior art of record, namely, the inhibition or downregulation Hepatitis C viral replication in an individual or cells. Therefore, the combination of references cannot anticipate or render obvious Claim 6 and 7 as a matter of law. Similarly, Claims 10, 12-14 and 36-39, which depend from non-obvious Claims 6 or 7, c cannot be found obvious under 35 U.S.C. §103 as a matter of law. MPEP

§2143.03.

In view of the amendments herein and the foregoing remarks, reconsideration and allowance of the claims as amended are respectfully requested. In order to submit a complete response, this paper is being filed concurrently with Notice of Appeal and the appropriate fee under 37 C.F.R. §1.17(b).

Should any issues remain after consideration of this response, Applicants request the Examiner contact their representatives at the number below.

Respectfully submitted,



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July 6, 2007
date

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